UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,636	08/22/2005	Gillian Lindy Durrant	052718/324523	4313

826 7590 03/16/2009

ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,636	DURRANT, GILLIAN LINDY	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,15,17-19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) *11,17-19 and 21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10, 12-13 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements .

DETAILED ACTION

1. Claims 10-13, 15, 17-19 and 21-25 are pending.

2. Applicant's election with traverse of Group I, claims 10-13 and 15, drawn to a combined preparation comprising a naked binding member, which binds to both SCR1 and SCR2 of CD55, and an active agent, said combined preparation being for simultaneous, separate or sequential use in the treatment of cancer, wherein said active agent is a chemotherapeutic agent, an antibody, a pain relief agent, an antibody, or an anti-emetic, and the species of antibody as the active agent, filed on 12/04/08, is acknowledged. Applicant did not indicate the reasons for the traversal. Since applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 11 (non-elected species), 17-19 and 21-25 (non-elected Groups) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

4. Claims 10, 12-13 nad 15 are under examination as they read on a combined preparation comprising a naked binding member, which binds to both SCR1 and SCR2 of CD55, and an active agent, said combined preparation being for simultaneous, separate or sequential use in the treatment of cancer, wherein said active agent is a chemotherapeutic agent, an antibody, a pain relief agent, an antibody, or an anti-emetic, and the species of antibody as the active agent.

5. Applicant's IDS, filed 5/27/08, is acknowledged.

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The specification on page 35, under Figure 1b, is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence.

The specification discloses the alignment of the three CDR peptides with CD55 that fail to comply with the sequence rule. Applicant is reminded of the sequence rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules. Correction is required.

7. Claim 13 is objected to because it depends from itself (i.e., claim 13). Further, the "anti-CEA", is missing the word "antibody".

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 10, 12-13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite "naked binding member which/that binds to both SCR1 and SCR2 of CD55", as part of the invention.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms that are common to the genus. That is, the specification provides neither a representative number of species (naked binding member which/that binds to both SCR1 and SCR2 of CD55) to describe the claimed genus, nor does it provide a description of structural features that are common to species (naked binding member which/that binds to both SCR1 and SCR2 of CD55). The specification provides no structural description of naked binding member which/that binds to both SCR1 and SCR2 of CD55 other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed naked binding member looks like. The specification's disclosure is inadequate to describe the claimed genus of naked binding member.

Applicant has disclosed only 791T/36 monoclonal antibody that binds to both SCR1 and SCR2 of CD0; therefore, the skilled artisan cannot envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. Claims 10, 12-13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for a combined preparation comprising a naked binding member, which binds to both SCR1 and SCR2 of CD55 and an active agent wherein the active agent is a chemotherapeutic agent, a pain relief agent, an antibody, or an anti-emetic in claim 10, and 12, an anti-CD20 antibody, an anti-VEGF antibody, an anti-CD171A antibody, An anti-CEA, anti-idiotypic mAb, an anti-HMFG anti-idiotypic mAb, an anti-EGFR antibody, or an anti-HER2 antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification under on page 38, under Results, discloses that binding of 791T/36 to SCR1 and SCR2 domains functionally inactivates CD55 leading to a 250% increase in C3b deposition. The specification on page 9, lines 27-31 discloses that previous studies have demonstrated that antibodies which target either SCR1 or SCR2 of CD55 failed to have any neutralization effect on CD55, an antibody which targets both SCR1 and SCR2 not only effectively neutralizes CD55 but is superior to a SCR3 neutralizing antibody.

While the claims recites naked binding member that binds to both SCR1 and SCR2 of CD55, the specification, under example 2, discloses the use of radiolabelled 791T/36 for imaging long term survival of recurrent colorectal cancer patients. Claim 15 requires the use of naked binding member that binds both SCR1 and SCR2 of CD55 for the treatment of cancer, the specification on page 39, lines 24-29, discloses survival was followed for 7 years and compared to a contemporary group of recurrent colorectal cancer patients. There were 12 long term survivors

(16%) in the patients who had received 791T/36 (radiolabelled, see table 1, page 40) where as in contrast only 1 out of 89 patients survived 7 years in the contemporary group. The specification on page 40, lines 6-15, discloses that the dose of radiolabel reaching the tumor is well below the level required to elicit tumor killing as a result of the radiolabel alone. It is therefor more likely that the antibody is inactivating CD55, allowing complement attack of residual tumor. As these patients only received a single intravenous dose of 791T/36 antibody the apparent survival benefit is very dramatic. Repeat injection with a humanized 791T/36 antibody may have an even more pronounced therapeutic benefit.

However, Applicant only administered radiolabelled 791T/36 antibody, no naked binding member, or humanized 791T/36 has been administered to any patient. While Applicant dismisses that the dose of radiolabel reaching the tumor is well below the level required to elicit tumor killing as a result of the radiolabel alone. However, Applicant concludes that it is therefor more likely that the antibody is inactivating CD55, allowing complement attack of residual tumor. However, the single dose of the antibody was administered and it is unclear how applicant concluded that the antibody is more likely inactivating CD55, allowing complement attack of residual tumor. Further, the effect applicant describing could be due to both the radioactive material and the antibody together. No evidence has been show that CD55 alone would enhance the long term survivor of colorectal cancer patients. It is unclear what type of medication/drugs the colorectal cancer patients have received during the 7 years period.

The specification fails to show the effect of naked binding member that binds to both SCR1 and SCR2 of CD55 on cancer treatment. No combination therapy was preformed in the specification. No naked binding member that binds to both SCR1 and SCR2 of CD55 was used to treat any disease including cancer. No disease was treated or detected using any combination therapy with any active agent, including any antibody in claim 10, any anti-idiotypic mAb, anti-CD20 antibodies, anti-VGEF antibodies, anti-CD171A antibodies, anti-CEA antibodies, anti-HMFG anti-idiotypic mAb, anti EGFR antibodies anti-HER2 antibodies in claim 13.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

12. Claim 10 is rejected under 35 U.S.C. 102(e) as being anticipated by US Pat. No. 7,267,821, as is evidenced by Spendlove et al (Eur. J. Immunol. 2000, 30:2944-2953).

The `821 patent teaches the use 791T/36 in combination with Tamoxifen on C170 growth (see col., 19, lines 56-57 and Fig. 14, Fig 16). The `821 patent further teaches 791T/36 in combination with Cisplatin (Fig. 11), 5-fluorouracil (Fig 13). While the `821 patent is silence with respect to binding to both SCR1 and SCR2 of CD55, the reference 791T/36 binds to both SCR1 and SCR2 of CD55 as is evidenced by Spendlove et al that the binding site of 791T/36 to the first two small consensus repeat (SCR) domains of the complement regulatory protein (CD55) that is overexpressed by a wide range of solid tumors (see abstract).

The reference teachings anticipate the claimed invention.

13. Claims 10, 12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Spendlove et al (Eur. J. Immunol. 2000, 30:2944-2953).

Spendlove et al teach mapping the binding site of 791T/36 to the first two small consensus repeat (SCR) domains of the complement regulatory protein (CD55) that is overexpressed by a wide range of solid tumors (see abstract). Spendlove et al teach the use of 5 μg/ml of 791T/36 mAb (see Fig. 5). Given the broadest reasonable interpretation of the claims and in the absence of disclosure that the active agent (antibody) is cannot be the same as the naked binding member, claim 10 recites a combined preparation comprising a naked binding member which binds to both SCR1 and SCR2 of CD55 and an antibody. Given that the 791T/36 which binds to both SCR1 and SCR2 of CD55, was used at 5 μg/ml, then there are multiple molecules of the 791T/36 antibodies in the given composition. Accordingly, the term "an antibody" would also read on 791T/36 antibody (naked binding member) combined with 791T/36 antibody (active agent).

Claim 15 is included because the 5 μg/ml of 791T/36 (composition) was used under physiological condition. Accordingly, the carrier in the composition must be pharmaceutically acceptable excipients, diluent or carrier.

The prior art product is the same as the claimed product and the intended uses "for the treatment of caner" do not carry patentable weight per se and the claims read on the active or essential ingredients of the "naked binding member that binds to both SCR1 and SCR2 of CD55) and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of the claimed compositions. Regardless, the composition of the Spendlove et al. reference is not incompatible with a therapeutic intention.

The reference teachings anticipate the claimed invention.

14. Claims 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Durrant et al (Jounal of the National Cancer Institute, 81(9): 688-696, 1989), as is evidenced by Spendlove et al (Eur. J. Immunol. 2000, 30:2944-2953).

Durrant et al teach a combination of MAbs C14, NCRC-23 and 791T/36 recognized 95% of gastric tumors. Combinations of either 791T/36 and C14 or 791T/36 and NCRC-11 recognized 80% of ovarian tumors. While the reference may be silence with as to the 791T/36 binds both SCR1 and SCR2 of CD55, the reference 791T/36 binds both SCR1 and SCR2 of CD55 as evidenced by Spendlove et al. Spendlove et al maps the binding site of 791T/36 to the first two small consensus repeat (SCR) domains of the complement regulatory protein (CD55) that is overexpressed by a wide range of solid tumors (see abstract).

The reference teachings anticipate the claimed invention.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 10, 12-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golay et al (Blood, 1 December 2001, Vol. 98, No. 12, pp. 3383-3389) in view of Spendlove et al (Eur. J. Imunol. 2000, 30:2944-2953) OR Spendlove et al (1999, Cancer Research 59,2282-2286, IDS reference G).

Golay et al teach that CD20 levels determine the in vitro susceptibiltiy to rituximab and complement of B-cell chronic lymphocytic leukemia: further regulation by CD55 and CD59 (see title). Complement-dependent cytotoxicity is thought to be an important mechanism of action of the anti-CD20 monoclonal antibody rituximab (see abstract). Golay et al teach that allthough CD55 and CD59 levels did not permit prediction of complement susceptibility, the functional block of these inhibitors demonstrated that they play an important role in regulating complement-dependent cytotoxicity (see abstract). The lysis of poorly responding B-CLL samples was increased 5- to 6-fold after blocking both CD55 and CD59, whereas that of high responders was essentially complete in the presence of a single blocking antibody. These data demonstate that CD20, CD55 and CD59 are important factors determining the in vitro response to rituximab and complement and indicate potential strategies to improve the clinical response to this biological therapy (see abstract). Golay et al teach that CD55 and/or CD59 block rituximab and complement-mediated lysis (see Fig. 5 and page 3386, 2nd col., 2nd ¶). Golay et al teach that this finding may be important in the context of resistance to rituximab in vivo, where increasing rituximab activity may allow elimination of residual resistant cells (see page 3389, 1st col., top ¶). Golay et al teach that the variability in the response of fresh leukemic cells to complement in

vitro may reflect the heterogeneity in the response of leukemic patients to this drug in vivo. Particularly for B-CLL, patients showing stronger lysis in vitro may be those more at risk of developing infusion-related side effects. Indeed, a relatively poor response of B-CLL patients to rituximab has been reported, as some cases of life-threatening tumor lysis syndrome, which would correlate with the data presented here. Golay et al propose that simple, reproducible, inexpensive, and rapid quantitative assay of CDC on fresh leukemic samples should be a valuable tool to predict the in vivo response of different patients. The need for a relatively small quantity of cells for this assay should allow its applicability also to neoplastic cells isolated from lymph node biopsies. Golay et al teach that their data strongly suggest that inhibiting the CD55 and/or DCD59 antigens in vivo could markedly improve the biologic activity of rituximab (see page 3389, last ¶). Golay et al teach the use of rituximab and functionally blocking anti-CD55 antibody (i.e., simultaneous) (see page 3384, under *Complement-mediated lysis*).

The claimed invention differs from the reference teachings only by the recitation that naked binding member, which binds to both SCR1 and SCR2 of CD55 in claim 10.

Spendlove et al (2000) teach mapping the binding site of 791T/36 mAb to the first two small consensus repeat (SCR) domains of the complement regulatory protein (CD55) that is overexpressed by a wide range of solid tumors (see abstract).

Spendlove et al (1999) have purified, characterized, cloned, and sequenced the 791Tgp72 antigen for tumor cells and shown that it is identical in sequence to CD55 (DAF). This molecule is normally expressed by cells to protect them from complement-mediated lysis. Spendlove et al teach that their previous studies have characterized this antigen as being overexpressed by a range of tumors, making it a good target for imaging and proving to be of prognostic significance in colorectal carcinoma (see page 2282, 2nd col., 1st full ¶).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti-CD55 antibody taught by Golay et al with the 791T/36 mAb taught by Spendlove et al to increase the mean lysis or increase CDC which leads to increasing rituximab activity and allow elimination of residual resistant cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because to improve the biologic activity of rituximab as taught by Golay et al.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. Claims 10, 12-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golay et al (Blood. 2000 Jun 15;95(12):3900-8) in view of Spendlove et al (Eur. J. Imunol. 2000, 30:2944-2953) OR Spendlove et al (1999, Cancer Research 59,2282-2286, IDS reference G).

Golay et al teaches that CD55 and CD59 can inhibit complement-mediated cell lysis. Golay et al showed that complement mediated lysis varied from 100% lysis to complete resistance on several Burkitt's lymphoma cell lines. Golay et al showed that by blocking CD55 with specific antibodies, CDC responses were increased, indicating that heterogeneity of rituximab responsiveness is in part, affected by complement regulatory protein. Golay et al concluded that CD55 can regulate complement-mediated lysis and is a most effective inhibitor on the resistant Karpas 422 cell line (see Fig. 9 and page 3905, under *CD55 and CD59 can inhibit complement-mediated cell lysis*). Fig. 9 showed increase cell death of cells treatment with rituximab and anti-CD55 antibody. Golay et al teach that cells were incubated with rituximab and blocking antibodies (i.e., simultaneous) (see page 3901, under *Complement-mediated cell lysis*). Golay et al concluded that novel and still more efficacious immunotherapeutic strategies could include either the combined administration of rituximab, together with blocking anti-CD55 antibodies, or the production of bispecific anti-CD20/CD55 reagents (see page 3907, last ¶).

The claimed invention differs from the reference teachings only by the recitation that naked binding member, which binds to both SCR1 and SCR2 of CD55 in claim 10.

Spendlove et al (2000) teach mapping the binding site of 791T/36 mAb to the first two small consensus repeat (SCR) domains of the complement regulatory protein (CD55) that is overexpressed by a wide range of solid tumors (see abstract).

Spendlove et al (1999) have purified, characterized, cloned, and sequenced the 791Tgp72 antigen for tumor cells and shown that it is identical in sequence to CD55 (DAF). This molecule is normally expressed by cells to protect them from complement-mediated lysis. Spendlove et al teach that their previous studies have characterized this antigen as being overexpressed by a range of tumors, making it a good target for imaging and proving to be of prognostic significance in colorectal carcinoma (see page 2282, 2nd col., 1st full ¶).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti-CD55 antibody taught by Golay et al with the 791T/36 mAb taught by Spendlove et al to increase the mean lysis or increase CDC which leads to increasing rituximab activity and allow elimination of residual resistant cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because to improve the biologic activity of rituximab as taught by Golay et al.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 3, 2009

/Maher M. Haddad/
Maher M. Haddad, Ph.D.
Primary Examiner
Technology Center 1600